

This Listing of Claims will replace all prior versions, and listings, of claims in the application.

In the claims:

Claims 1-60 (Canceled)

61. (Currently amended) An isolated nucleic acid molecule that encodes a fusion protein, said molecule comprising: a polynucleotide sequence encoding an OB polypeptide that is capable of modulating body weight; and at least one polynucleotide sequence encoding at least one polyaminoacid polymer, said at least one polynucleotide sequence joined in frame to said polynucleotide sequence encoding an OB polypeptide, also encodes one or more polyaminoacid polymers attached to said OB polypeptide, said nucleic acid optionally in a pharmaceutical carrier, wherein said OB polypeptide encoded by said isolated nucleic acid comprises the an amino acid sequence set out in:

- (a) SEQ ID NO:2;
- (b) amino acids 22-167 of SEQ ID NO:2;
- (c) SEQ ID NO:4; or
- (d) amino acids 22-167 of SEQ ID NO:4.

62. (Currently amended) An isolated nucleic acid molecule that encodes a fusion protein, said molecule comprising: a polynucleotide sequence encoding an OB polypeptide that is capable of modulating body weight; and at least one polynucleotide sequence encoding at least one polyaminoacid polymer, said at least one polynucleotide sequence joined in frame to said polynucleotide sequence encoding an OB polypeptide, also encodes one or more polyaminoacid polymers attached to said OB polypeptide, said nucleic acid optionally in a pharmaceutical carrier, wherein said OB polypeptide encoded by said isolated nucleic acid comprises the an amino acid sequence set out in:

- (a) SEQ ID NO:5;
- (b) amino acids 22-166 of SEQ ID NO:5;
- (c) SEQ ID NO:6; or
- (d) amino acids 22-166 of SEQ ID NO:6.

Claim 63 (Currently amended) An isolated nucleic acid molecule that encodes a fusion protein, said molecule comprising: a polynucleotide sequence encoding an OB polypeptide that is capable of modulating body weight; and at least one polynucleotide sequence encoding at least one polyaminoacid polymer, said at least one polynucleotide sequence joined in frame to said polynucleotide sequence encoding an OB polypeptide, also encodes one or more polyaminoacid polymers attached to said OB polypeptide, said nucleic acid optionally in a pharmaceutical carrier, wherein said OB polypeptide has 83 percent or greater amino acid identity to the an OB polypeptide amino acid sequence set out in SEQ ID NO:2, 4, 5, or 6.

64. (Currently amended) An isolated nucleic acid molecule that encodes a fusion protein, said molecule comprising: a polynucleotide sequence encoding an OB polypeptide that is capable of modulating body weight; and at least one polynucleotide sequence encoding at least one polyaminoacid polymer, said at least one polynucleotide sequence joined in frame to said polynucleotide sequence encoding an OB polypeptide, also encodes one or more polyaminoacid polymers attached to said OB polypeptide, said nucleic acid optionally in a pharmaceutical carrier, wherein said OB polypeptide encoded by said isolated nucleic acid is an OB polypeptide ~~variant comprising~~ comprises amino acids 22-167 of SEQ ID NO:4 in which one or more amino acids are selected from the group consisting of amino acids 53, 56, 71, 85, 89, 92, 95, 98, 110, 118, 118, 121, 122, 126, 127, 128, 129, 132, 139, 157, ~~156,~~ 159, 163, and 166, according to the numbering of SEQ ID NO:4, is are substituted with a conserved amino acid.

65. (Currently amended) An isolated nucleic acid molecule that encodes a fusion protein, said molecule comprising: a polynucleotide sequence encoding an OB polypeptide that is capable of modulating body weight; and at least one polynucleotide sequence encoding at least one polyaminoacid polymer, said at least one polynucleotide sequence joined in frame to said polynucleotide sequence encoding an OB polypeptide, also encodes one or more polyaminoacid polymers attached to said OB polypeptide, said nucleic acid optionally in a pharmaceutical carrier, wherein said OB polypeptide encoded by said isolated nucleic acid is an OB polypeptide ~~variant comprising~~ comprises amino acids 22-167 of SEQ ID NO:4 in which one or more amino

acids are selected from the group consisting of amino acids 53, 56, 71, 85, 89, 92, 95, 98, 110, 118, 121, 122, 126, 127, 128, 129, 132, 139, 157, 159, ~~and~~ 163, and 166, according to the numbering of SEQ ID NO:4, ~~is~~ are substituted with the particular amino acid present at the corresponding position in SEQ ID NO:2.

66. (Currently amended) An isolated nucleic acid molecule that encodes a fusion protein, said molecule comprising: a polynucleotide sequence encoding an OB polypeptide that is capable of modulating body weight; and at least one polynucleotide sequence encoding at least one polyaminoacid polymer, said at least one polynucleotide sequence joined in frame to said polynucleotide sequence encoding an OB polypeptide, ~~also encodes one or more polyaminoacid polymers attached to said OB polypeptide, said nucleic acid optionally in a pharmaceutical carrier,~~ wherein said OB polypeptide ~~encoded by said isolated nucleic acid is an OB polypeptide variant comprising~~ comprises amino acids 22-167 of SEQ ID NO:6 in which one or more amino acids are selected from the group consisting of amino acids 52, 55, 70, 84, 88, 91, 94, 97, 109, 117, 120, 121, 125, 126, 127, 128, 131, 138, 156, 158, 162, and 165, according to the numbering of SEQ ID NO:6, ~~is~~ are substituted with a conserved amino acid.

67. (Currently amended) An isolated nucleic acid molecule that encodes a fusion protein, said molecule comprising: a polynucleotide sequence encoding an OB polypeptide that is capable of modulating body weight; and at least one polynucleotide sequence encoding at least one polyaminoacid polymer, said at least one polynucleotide sequence joined in frame to said polynucleotide sequence encoding an OB polypeptide, ~~also encodes one or more polyaminoacid polymers attached to said OB polypeptide, said nucleic acid optionally in a pharmaceutical carrier,~~ wherein said OB polypeptide ~~encoded by said isolated nucleic acid is an OB polypeptide variant comprising~~ comprises amino acids 22-167 of SEQ ID NO:6 in which one or more amino acids are selected from the group consisting of amino acids 2, 55, 70, 84, 88, 91, 94, 97, 109, 117, 120, 121, 125, 126, 127, 128, 131, 138, 156, 158, 162, and 165, according to the numbering of SEQ ID NO:6 ~~is~~ are substituted with the particular amino acid present at the corresponding position in SEQ ID NO:5.

Claim 68 (Canceled)

69. (Currently amended) ~~The~~ A nucleic acid ~~of-molecule according to~~ any one of claims 61-67 and 89-94, wherein at least one of said at least one polyaminoacid ~~polymers~~ polymer is N-terminally attached to said OB polypeptide.

70. (Currently amended) ~~The~~ A nucleic acid ~~of-molecule according to~~ any one of claims 61-67 and 89-94, wherein at least one of said at least one polyaminoacid ~~polymers~~ polymer is C-terminally attached to said OB polypeptide.

71. (Currently amended) ~~The~~ A nucleic acid ~~of-molecule according to~~ any one of claims 61-67 and 89-94, wherein said nucleic acid molecule is selected from the group consisting of DNA and RNA.

72. (Currently amended) ~~The~~ A nucleic acid ~~of-molecule according to~~ any one of claims 61-67 and 89-94, wherein said nucleic acid molecule is detectably labeled.

73. (Currently amended) ~~The~~ A cloning vector comprising a nucleic acid ~~of-molecule according to~~ any one of claims 61-67 and 89-94, wherein said nucleic acid is detectably labeled.

74. (Currently amended) An expression ~~construct~~ vector comprising a nucleic acid ~~of-molecule according to~~ any one of claims 61-67 and 89-94, ~~operatively associated with~~ linked to an expression control sequence.

75. (Currently amended) An expression ~~construct~~ of vector according to claim 74, wherein said expression control sequence is selected from the group consisting of: a cytomegalovirus hCMV immediate early gene; the early or late promoters of SV40, CMV, vaccinia, polyoma, or adenovirus; the lac system; the trp system; the TAC system; the TRC system; the LTR system; the major operator and promoter regions of phage λ ; the control regions of fd coat protein; the

promoter for 3-phosphoglycerate kinase; the promoters of acid phosphatase; the AOX 1 promoter of the methylotrophic yeast; and the promoters of the yeast α -mating factors.

76. (Previously presented) A unicellular host transfected with a cloning vector of claim 73.

77. (Currently amended) A host cell transformed with an expression ~~construct~~ vector of claim 74.

78. (Currently amended) The host cell of claim 77, wherein said host cell is selected from the group consisting of *E. coli* cells, *Pseudomonas* cells, *Bacillus* cells, *Streptomyces* cells, yeast cells, ~~*Pichia* yeasts~~ *Pichia* cells, *Saccharomyces* cells, *Candida* cells, *Hansenula* cells, *Torulopsis* cells, CHO cells, R1.1 cells, B-W cells, L-M cells, COS-1 cells, COS-7 cells, BSC1 cells, BSC40 cells, BMT10 ~~and~~ cells, Sf9 cells, and plant cells, insect cells, and human cells in tissue culture.

79. (Currently amended) A method for preparing a fusion protein comprising an OB polypeptide comprising:

- (a) culturing a host cell ~~of~~ according to claim 76 under conditions that allow the expression of said ~~OB polypeptide-fusion protein~~; and
- (b) recovering the expressed ~~OB polypeptide-fusion protein~~.

80. (Previously presented) The method of claim 79, wherein said host cell is a bacterial cell.

81. (Previously presented) The method of claim 79 wherein said host cell is a yeast cell.

82. (Currently amended) The method of claim 79, further comprising:

- (c) chromatographing ~~the polypeptide~~ said fusion protein on a Ni-chelating column; and
- (d) purifying ~~the polypeptide~~ said fusion protein by gel filtration.

83. (Currently amended) the method of claim 82, further comprising after step (c) and prior to step (d), chromatographing ~~the OB polypeptide~~ said fusion protein on a strong cation exchanger column.

84. (Currently amended) A method for preparing a fusion protein comprising an OB polypeptide comprising:

(a) culturing a host cell ~~of~~ according to claim 77 under conditions that allow the expression of said ~~OB polypeptide~~ fusion protein; and

(b) recovering the expressed ~~OB polypeptide~~ fusion protein.

85. (Previously presented) The method of claim 84, wherein said host cell is a bacterial cell.

86. (Previously presented) The method of claim 84 wherein said host cell is a yeast cell.

87. (Currently amended) The method of claim 84, further comprising:

(c) chromatographing ~~the polypeptide~~ said fusion protein on a Ni-chelating column;
and

(d) purifying ~~the polypeptide~~ said fusion protein by gel filtration.

88. (Currently amended) The method of claim 84, further comprising:

(c) chromatographing ~~the polypeptide~~ said fusion protein on a Ni-chelating column;
and

(d) purifying ~~the polypeptide~~ said fusion protein by gel filtration.

89. (New) An isolated nucleic acid molecule according to claim 61, wherein said at least one polynucleotide sequence comprises two or more polynucleotide sequences, and further wherein said at least one polyaminoacid polymer comprises two or more polyaminoacid polymers.

90. (New) A composition comprising an isolated nucleic acid molecule according to claim 61 in

a pharmaceutical carrier.

91. (New) An isolated nucleic acid molecule according to claim 62, wherein said at least one polynucleotide sequence comprises two or more polynucleotide sequences, and further wherein said at least one polyaminoacid polymer comprises two or more polyaminoacid polymers.

92. (New) A composition comprising an isolated nucleic acid molecule according to claim 62 in a pharmaceutical carrier.

93. (New) An isolated nucleic acid molecule according to claim 63, wherein said at least one polynucleotide sequence comprises two or more polynucleotide sequences, and further wherein said at least one polyaminoacid polymer comprises two or more polyaminoacid polymers.

94. (New) A composition comprising an isolated nucleic acid molecule according to claim 63 in a pharmaceutical carrier.

95. (New) An isolated nucleic acid molecule according to claim 64, wherein said at least one polynucleotide sequence comprises two or more polynucleotide sequences, and further wherein said at least one polyaminoacid polymer comprises two or more polyaminoacid polymers.

96. (New) A composition comprising an isolated nucleic acid molecule according to claim 64 in a pharmaceutical carrier.

97. (New) An isolated nucleic acid molecule according to claim 65, wherein said at least one polynucleotide sequence comprises two or more polynucleotide sequences, and further wherein said at least one polyaminoacid polymer comprises two or more polyaminoacid polymers.

98. (New) A composition comprising an isolated nucleic acid molecule according to claim 65 in a pharmaceutical carrier.

99. (New) An isolated nucleic acid molecule according to claim 66, wherein said at least one polynucleotide sequence comprises two or more polynucleotide sequences, and further wherein said at least one polyaminoacid polymer comprises two or more polyaminoacid polymers.

100. (New) A composition comprising an isolated nucleic acid molecule according to claim 66 in a pharmaceutical carrier.

101. (New) The method of claim 79, wherein said host cell is a mammalian cell.

102. (New) The method of claim 84, wherein said host cell is a mammalian cell.